REMARKS

Applicants respectfully request reconsideration of this application in view of the above Amendment and the following remarks.

Claims 1, 23, and 44 have been amended to provide that the encoded GHRH corresponds to SEQ ID NO.: 6. Applicants respectfully direct the Examiner's attention to the Office Action mailed on May 9, 2006, Page 6, in which the Examiner indicated that the specification disclosed those 48 encoded GHRH sequences corresponding to SEQ ID NO.: 6 and that the specification showed that Applicants were in possession of those GHRH sequences of SEQ ID NO.: 6. For the purpose of complying with the restriction requirement of January 11, 2006, Applicants have also amended Claims 1, 23, and 44 to provide that the encoded GHRH corresponds to SEQ ID NO.: 1 in particular.

Claims 1, 23, and 44 have also been amended to provide that the constant current electrical pulse is maintained under a threshold to allow one to reduce cell heating and create less cell death. Support for this amendment is found in the Specification at Paragraph 156.

Claims 30 and 48 have been amended to correct the spacing in "SEQID." Claims 28, 30, 34, 37, 38, and 40 – 42 have been amended to correct the dependency of these claims, which was mistakenly listed as dependency from Claim 26, rather than independent Claim 23. Finally, Claims 20, 39, and 57 have been cancelled.

Pending in this application are Claims 1-4, 7-9, 11, 15-19, 22, 23, 26-28, 30, 34-38, 40-45, 47, 48, and 52-56.

I. Claim Objections

The Examiner has objected to Claims 1, 23, and 44 as being "ungrammatical." Applicants have amended these claims to delete the terminology the Examiner has objected to.

The Examiner has suggested the removal of the parentheses around "SEQ ID NO.: 1" in Claims 1, 20, 23, 39, 44, and 57. Applicants have amended Claims 1, 23, and 44 in accordance with the Examiner's suggestions. Claims 20, 39, and 57 have been canceled.

Finally, the Examiner has objected to Claims 30, 48, and 86 and requested the insertion of a space within the term "SEQID." Applicants have amended Claims 30 and 48 in accordance with the Examiner's suggestion. Claim 86, being withdrawn, has not been amended.

In view of these amendments, Applicants respectfully request that the Examiner withdraw the claim objections.

II. 35 U.S.C. §112, First Paragraph, New Matter

Claims 1-4, 7-9, 11, 15-19, 22, 23, 26-28, 30, 34-38, 40-45, 47, 48, and 52-56 stand rejected under 35 U.S.C. §112, first paragraph, for containing new matter that the Examiner asserts is not described in the specification. The Examiner asserts that the claim limitation "95% identical to (SEQ ID NO.: 1)" is not supported in the specification. Applicants have deleted this claim terminology from independent Claims 1, 23, and 44. In view of this, Applicants respectfully request that the Examiner withdraw these claim rejections.

III. 35 U.S.C. §112, First Paragraph, Written Description

Claims 1-4, 7-9, 11, 15-19, 22, 23, 26-28, 30, 34-38, 40-45, 47, 48, and 52-56 stand rejected under 35 U.S.C. §112, first paragraph, for failing to comply with the written description requirement. The Examiner asserts that the specification does not disclose sufficient examples and characteristics to support claiming the genus of "synthetic muscle-specific promoters." Applicants continue to respectfully disagree. The Examiner has asserted on Page 5 of the current Office Action that the issue is "whether or not the genus was adequately described." Applicants assert that, in view of the material described in the specification and that knowledge that is possessed by those of skill in the art, this genus of synthetic, muscle-specific promoters has been adequately described.

First, Applicants respectfully assert that those of skill in the art would clearly understand what is meant by "synthetic" promoters. Those individuals skilled in the art would likewise understand what is meant by "muscle-specific" promoters. The arts of both creating synthetic promoters and using promoters that are specific to a particular tissue are well-known and do not require further elaboration in the specification, particularly in view of Applicants' citation to

three different references in Table 2 of the Specification providing additional background support: Draghia-Akli et al., 1999, Draghia-Akli et al., 2002b, and Li et al., 1999. Thus, because this information is known to those of skill in the art, it is not necessary for Applicants to expressly list multiple specific examples or detailed descriptions of characteristics and structures. The claims clearly require that the promoters be (1) synthetic and (2) muscle-specific. Additional information is not required to demonstrate that Applicants were in possession of these promoters because these types of promoters are well-known in the art and do not require further description in the specification.

Nevertheless, Applicants respectfully assert that the specification provides ample description of promoters that are synthetic and muscle-specific. In particular, Paragraph 126 discusses synthetic promoters and their use within the claimed nucleic acid expression construct. Paragraph 127 discusses the importance of using promoters that are specific to a particular tissue because it will effectively direct the expression of the DNA segment within the targeted tissue. The Specification at Paragraph 127 provides the following guidance:

> Those of skill in the art of molecular biology generally know the use of promoters, enhancers, and cell type combinations for protein expression. The promoters employed may be constitutive, tissue-specific, inducible, and/or useful under the appropriate conditions to direct high level expression of the introduced DNA segment, such as is advantageous in the large-scale production of recombinant proteins and/or peptides. The promoter may be heterologous or endogenous.

Furthermore, Paragraph 130 provides numerous examples of tissue-specific promoters and enhancers. These eight (8) different examples, as well as the references cited with additional information, convey the type of structures and characteristics that support a full description of this type of promoter. As stated in Paragraph 130, "[t]he identity of tissue-specific promoters or elements, as well as assays to characterize their activity, is well known to those of skill in the art." The Specification's citation to eight different specific examples, as well as the references that fully describe them, clearly indicates that tissue-specific promoters are well known in the art and do not have to be further described to support Applicants' possession of them.

In addition to the material discussed above, Paragraph 131 provides a detailed description of the synthetic, muscle-specific promoter. The Specification at Paragraph 131 indicates that the

synthetic, muscle-specific promoter SPc5-12 contains "a proximal serum response element ("SRE") from skeletal α-actin, multiple MEF-2 sites, MEF-1 sites, and TEF-1 binding sites." This is clearly a description of identifying structural characteristics. The Specification also provides that SPc5-12 "greatly exceeds the transcriptional potencies of natural myogenic promoters." Thus, the structural elements described are clearly correlated with the function of improving transcriptional potency.

Finally, the Specification at Paragraph 131 describes the National Center for Biotechnology Information ("NCBI") GenBank database or the NCBI PubMed site and indicates that a "skilled artisan is aware that these databases may be utilized to obtain sequences or relevant literature related to the present invention." People skilled in this art are well aware that there is a multitude of information pertaining to these types of promoters available through such databases and web sites. Thus, it is abundantly clear that Applicants are not required to describe the entire genus of synthetic, muscle-specific promoters in redundant, unnecessary detail. Those of skill in the art know what a "synthetic" promoter is and what a "muscle-specific" promoter is and would fully understand the extent of this claimed genus. The Specification provides adequate description in addition to this common knowledge.

In view of these reasons, Applicants respectfully assert that the genus "synthetic, muscle-specific promoters" is adequately described in the Specification to fulfill the written description requirement.

IV. 35 U.S.C. §103(a)

A. Schwartz in view of Aihara and Simon

Claims 1-4, 7-9, 11, 18-19, 22, 23, 26-28, 30, 37-38, 40-45, 47, 48, and 55-56 stand rejected under 35 U.S.C. §103(a) as being unpatentable over International Patent Publication No. WO 2002/061037 to Schwartz et al. ("Schwartz") in view of the Nature Biotech. Publication by Aihara et al. ("Aihara") and U.S. Patent No. 6,928,318 to Simon ("Simon"). The Examiner asserts that Schwartz teaches the injection of a nucleic acid represented by SEQ ID NO.: 11 and that Aihara teaches electroporation at the injection site. In the previous response filed by

Applicants, Applicants argued that Schwartz in combination with Aihara did not teach the use of a constant current pulse in electroporation. In response to these arguments, the Examiner has sited an additional reference, Simon, which assertedly teaches the use of a constant current pulse in electroporation. Applicants respectfully assert that Simon does not teach the use of a constant current electrical pulse that meets the limitations of the claims as amended.

Claims 1, 23, and 44 have been amended to provide that, in the claimed step of applying a **constant current electrical pulse** to the plurality of electrodes, the constant current pulse is **maintained under a threshold** to allow one to reduce cell heating and create less cell death. Support for this amendment is found in Paragraph 156 of the Specification.

Simon does not teach maintaining a constant current pulse under a threshold to enable the user to reduce cell heating and create less cell death. Simon's electroporation device records electrical parameters concurrently with biological responses only to correlate them and assess the performance of the system. See Simon, col. 5, l. 59 – col. 6, l. 11. Thus, Simon's system provides no teaching of maintaining the actual constant current electrical pulse below a threshold. This is significantly different from the claims, which require maintaining the constant current electrical pulse below a threshold to reduce cell heating and create less cell death. Because Simon is only concerned with the correlation of electrical parameters with biological responses and not with the avoidance of cell heating and cell death, Simon's teachings with regard to electroporation cannot meet the claim limitations. There is nothing in Simon that would teach or suggest maintaining the constant current electrical pulse below a threshold, which is required by the claims.

For these reasons, Claims 1-4, 7-9, 11, 18-19, 22, 23, 26-28, 30, 37-38, 40-45, 47, 48, and 55-56 are patentable over Schwartz in view of Aihara and Simon.

B. Schwartz in view of Aihara, Simon, and Fewell

Claims 15-17, 34-36, and 52-54 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Schwartz in view of Aihara, Simon, and U.S. Patent Publication No. 2003/0109478 to Fewell ("Fewell"). These claims pertain to the use of a transfection-facilitating

polypeptide, which the Examiner asserts is taught by Fewell. Applicants respectfully assert that Schwartz, Aihara, Simon, and Fewell in combination do not teach or suggest all of the limitations of the claimed subject matter, as amended.

In particular, the Examiner cites to Simon as assertedly teaching constant current electroporation. However, Claims 1, 23, and 44 have been amended to provide that, in the claimed step of applying a constant current electrical pulse to the plurality of electrodes, the constant current pulse is maintained under a threshold to allow one to reduce cell heating and create less cell death. By contrast, Simon does not teach maintaining a constant current pulse under a threshold to enable the user to reduce cell heating and create less cell death. Simon's electroporation device records electrical parameters concurrently with biological responses only to correlate them and assess the performance of the system. See Simon, col. 5, l. 59 – col. 6, l. 11. Thus, Simon's system provides no teaching of maintaining the actual constant current electrical pulse below a threshold. This is significantly different from the claims, which require maintaining the constant current electrical pulse below a threshold to reduce cell heating and create less cell death. Because Simon is only concerned with the correlation of electrical parameters with biological responses and not with the avoidance of cell heating and cell death, Simon's teachings with regard to electroporation cannot meet the claim limitations. There is nothing in Simon that would teach or suggest maintaining the constant current electrical pulse below a threshold, which is required by the claims.

For these reasons, Claims 15-17, 34-36, and 52-54 are patentable over Schwartz in view of Aihara, Simon, and Fewell.

V. Double Patenting

A. U.S. Patent No. 6,423,693, in view of Schwartz and Simon

Claims 1-4, 7-9, 11, 18-19, 22, 23, 26-28, 30, 37-38, 40-45, 47, 48, and 55-56 stand rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Claims 21-23 of U.S. Patent No. 6,423,693 ("the '693 Patent"), in view of Schwartz and Simon. The Examiner asserts that Claims 21-23 of the '693 Patent pertain to methods for

delivering an expression vector encoding GHRH, that Schwartz teaches SEQ ID NO.: 1 and a synthetic, muscle-specific promoter, and that Simon teaches constant current electroporation. Applicants respectfully disagree and assert that the '693 Patent, Schwartz, and Simon in combination do not teach or suggest all of the subject matter of the amended claims.

In particular, the Examiner cites to Simon as assertedly teaching constant current electroporation. However, Claims 1, 23, and 44 have been amended to provide that, in the claimed step of applying a constant current electrical pulse to the plurality of electrodes, the constant current pulse is maintained under a threshold to allow one to reduce cell heating and create less cell death. By contrast, Simon does not teach maintaining a constant current pulse under a threshold to enable the user to reduce cell heating and create less cell death. Simon's electroporation device records electrical parameters concurrently with biological responses only to correlate them and assess the performance of the system. See Simon, col. 5, l. 59 – col. 6, l. 11. Thus, Simon's system provides no teaching of maintaining the actual constant current electrical pulse below a threshold. This is significantly different from the claims, which require maintaining the constant current electrical pulse below a threshold to reduce cell heating and create less cell death. Because Simon is only concerned with the correlation of electrical parameters with biological responses and not with the avoidance of cell heating and cell death, Simon's teachings with regard to electroporation cannot meet the claim limitations. There is nothing in Simon that would teach or suggest maintaining the constant current electrical pulse below a threshold, which is required by the claims.

For these reasons, Claims 1-4, 7-9, 11, 18-19, 22, 23, 26-28, 30, 37-38, 40-45, 47, 48, and 55-56 are patentably distinct from Claims 21-23 of the '693 Patent, in view of Schwartz and Simon.

B. U.S. Patent No. 6,423,693, in view of Schwartz, Simon, and Fewell

Claims 15-17, 34-36, and 52-54 stand rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Claims 21-23 of U.S. Patent No. 6,423,693 ("the '693 Patent"), in view of Schwartz, Simon, and Fewell. The Examiner asserts that Claims 21-23 of the '693 Patent pertain to methods for delivering an expression vector

encoding GHRH, that Schwartz teaches SEQ ID NO.: 1 and a synthetic, muscle-specific promoter, that Simon teaches constant current electroporation, and that Fewell teaches a transfection-facilitating polypeptide. Applicants respectfully disagree and assert that the '693 Patent, Schwartz, Simon, and Fewell in combination do not teach or suggest all of the subject matter of the amended claims.

In particular, the Examiner cites to Simon as assertedly teaching constant current electroporation. However, Claims 1, 23, and 44 have been amended to provide that, in the claimed step of applying a constant current electrical pulse to the plurality of electrodes, the constant current pulse is maintained under a threshold to allow one to reduce cell heating and create less cell death. By contrast, Simon does not teach maintaining a constant current pulse under a threshold to enable the user to reduce cell heating and create less cell death. Simon's electroporation device records electrical parameters concurrently with biological responses only to correlate them and assess the performance of the system. See Simon, col. 5, l. 59 – col. 6, l. 11. Thus, Simon's system provides no teaching of maintaining the actual constant current electrical pulse below a threshold. This is significantly different from the claims, which require maintaining the constant current electrical pulse below a threshold to reduce cell heating and create less cell death. Because Simon is only concerned with the correlation of electrical parameters with biological responses and not with the avoidance of cell heating and cell death, Simon's teachings with regard to electroporation cannot meet the claim limitations. There is nothing in Simon that would teach or suggest maintaining the constant current electrical pulse below a threshold, which is required by the claims.

For these reasons, Claims 15-17, 34-36, and 52-54 are patentably distinct from Claims 21-23 of the '693 Patent, in view of Schwartz, Simon, and Fewell.

VI. Conclusion

Applicant respectfully submits that, in light of the foregoing comments and amendments, all pending claims are now in condition for allowance. A Notice of Allowance is therefore requested.

If the Examiner has any other matters which pertain to this Application, the Examiner is encouraged to contact the undersigned to resolve these matters by Examiner's Amendment where possible.

Respectfully submitted,

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